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U. S. DEPARTMENT OF
AGRICULTURE

FARMERS' BULLETIN No. 1593

TREMBLES



THE DEPARTMENT OF AGRICULTURE has received many requests for information on trembles or milk sickness. Although the data on this subject are available in many special and somewhat detailed publications to which correspondents can be referred, most of these persons do not desire details, but a summary of the facts regarding the disease.

To furnish such a summary this bulletin has been prepared. It describes the cause of the disease, means of prevention, and other essential facts. The comparatively few people who desire further particulars are referred to the more technical papers. Full bibliographies are given in the papers by Jordan and Harris, and Wolf, Curtis, and Kaupp, which are cited in the text of this bulletin.

Washington, D. C.

Issued June, 1929

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TREMBLES¹

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THE NAMES TREMBLES and MILK SICKNESS (or "milk-sick," as it was more commonly known in the early part of the nineteenth century) have been applied to a disease which was first definitely recognized in the States along the Ohio River, and was very common in the early days of the settlement of that region. It not only produced tedious and protracted illnesses but many fatalities. So numerous, in fact, were these cases, that it appeared as almost an epidemic in some places, causing so many deaths that some settlements were abandoned.

This disease was recognized as a distinct entity early in the nineteenth century, although it is probable that many of the so-called milk-sickness cases were caused by other diseases, such as malaria and typhoid fever.

While it is stated that the disease existed in North Carolina prior to 1776, the first published statement was by Dr. Daniel Drake, a distinguished physician of Ohio,² in 1810, who gave the symptoms in some detail. These symptoms included lassitude, pains in the legs, loss of appetite, obstinate constipation, vomiting, and a breath "peculiarly disgusting and even loathsome." He stated that the disease affected both sexes and all ages, and sometimes continued for months, and that patients after recovery are liable to recurrences. He said that it occurred in "aguish" situations, and that since its appearance intermittent diseases declined. (It seems possible that the diagnosis of trembles or milk sickness as distinct from malarial disease may have resulted in an apparent diminution of "intermittent diseases.")

¹ Instead of the more common name "milk sickness" the name "trembles" is used by direction of the Director of Scientific Work on the ground that milk is a carrier and not the cause of the disease. Trembles has also been referred to as milk-sick, sick stomach, sick stomach or milk sickness, trembles or milk sickness, and epidemic fever.

² DRAKE, D. NOTICES CONCERNING CINCINNATI. 60 p. Cincinnati. 1810. (Reprint in Quart. Pub. Hist. and Phil. Soc. Ohio, v. 3, no. 1-2, 1908.)

Drake's account of the disease was of that seen in human patients. He stated, however, that it occurred also in horses, cows, sheep, and dogs. Drake gave no name to the disease and, apparently, did not at that time connect it with milk. At the time of his first publication the name most commonly applied was "sick stomach." Later a number of names were given, among them being "puking fever," "fall poison," "swamp sickness," "river sickness," "tires," "slows," "bilious sick stomach," and "trembles." These names evidently arose from ideas in regard to the origin of the disease or from its symptoms. Wherever it was commonly believed that the human cases had their origin in milk or butter from diseased cows, the term "milk sickness" came into common use. In some localities the term "trembles" was generally used, for it was found that affected animals trembled more or less violently after exercise, and similar trembling was noted in many human cases. Many cattle buyers in regions where trembles occurred required that, before contracts were completed, the animals be driven a stipulated distance in order to make certain that they did not have the disease.

It will be remembered that Drake spoke of the "peculiarly disgusting breath," and many physicians claimed that by this they could diagnose cases of trembles or milk sickness as soon as they stepped into the houses of the patients. Dr. W. E. Walsh, of Morris, Ill.,³ recognized the odor as due to acetone, reported acetone and diacetic acid in the urine of some patients, and diagnosed the disease as an acidosis. This odor of acetone was found to be characteristic of many of the experimental animals of the Department of Agriculture.

As the clinical thermometer came into common use among physicians, it was found that persons affected by the disease generally had a subnormal temperature.

In the course of the nineteenth century there was a large body of literature on the subject, the papers for the most part treating of the human disease, because of the seriousness of its effect in communities. It was known, however, that there were many losses of livestock, especially of cattle.

The disease was most common in Ohio, Indiana, and Illinois, but it also occurred in Kentucky, Tennessee, and North Carolina, and there have been cases in Virginia and Georgia. It has been reported as far west as Missouri and as far north as Michigan.

CAUSE OF THE DISEASE

Many theories have been advanced in regard to the cause of the disease; some were founded on more or less baseless guesswork; others had some foundation in fact. The cases in the neighborhood of the Ohio River occurred largely in lowlands near the sluggish streams of that region. Because of the proximity to swampy areas it was supposed by some persons that the disease was produced either by an organism from the stagnant waters or by poisonous gases arising from them.

³ WALSH, W. E. CLINICAL REPORT OF THE REAPPEARANCE OF THE ONCE COMMON AND FATAL MILK SICKNESS OR "MILK-SICK," WITH SUCCESSFUL RATIONAL TREATMENT DEDUCED FROM CLINICAL FINDINGS. Ill. Med. Jour. 15: 422-425. 1909.

In North Carolina it was commonly believed that the cause was an emanation from the soil. Some persons claimed that the gas arises in the night and settles on the vegetation, that cattle are poisoned when they feed on the vegetation at night or early in the morning, and that if the animals are kept from the pastures at night and not turned out too early in the morning, they are not poisoned. Hay lying on the ground was thought to become poisonous. Dr. D. D. Owen, when State geologist of Kentucky, had a similar but more elaborate theory. He said that in trembles regions the soils contained pyrite-bearing shales and clays. In the decomposition of the iron pyrite, oxygen was taken from the atmosphere, and the waters were made astringent by the sulphate of aluminum and the double sulphate of aluminum and iron which were formed; he thought also that the vegetation became astringent by the absorption of these salts. Because of this process, the quantity of oxygen in the atmosphere near the ground would be lessened. Therefore when cattle grazed with their heads near the ground they would, according to the theory, suffer from insufficiency of oxygen, and the disease was caused by the combined effect of the lack of oxygen and the astringent water. In some localities certain areas were recognized as especially poisonous, and fences were erected to keep cattle from grazing in those places.

Many suggested a plant origin for the disease. Mushrooms and other fungi were suspected. Poison ivy was mentioned by a number of authors. However, the plant most frequently mentioned as responsible for the disease was white snakeroot (*Eupatorium urticæfolium*), known to earlier botanists as *E. ageratoides*.

With the development of the science of bacteriology, many sought the cause in a disease-producing organism. In 1909 Jordan and Harris⁴ published a comprehensive paper on the subject in which they suggested the probability that the disease was caused by an organism found in the soil. They called the organism *Bacillus lactimorbi*. This bacillus was found by Luckhardt on white snakeroot and other plants.

The work of Jordan and Harris⁴ and a publication by Crawford⁵ in the preceding year, in which he concluded that white snakeroot was not toxic, seemed so conclusive that for a few years the plant theory was abandoned by most people interested in the subject. There were some, however, in regions where trembles occurred, who still believed that white snakeroot was at the bottom of the trouble, and further experimentation was demanded. This was undertaken by the United States Department of Agriculture and resulted in conclusive proof that feeding white snakeroot to animals would produce all the typical symptoms of trembles. This was true even when the plant was sterilized, thus disposing of the bacterial theory. The fact that the disease has been produced in animals by extracts of white snakeroot prepared by methods which would make them undoubtedly sterile is additional proof that the bacterial theory is untenable. Similar re-

⁴ JORDAN, E. O., and HARRIS, N. M. MILK SICKNESS. *Jour. Infect. Diseases* 6: 401-491, illus. 1909.

⁵ CRAWFORD, A. C. THE SUPPOSED RELATIONSHIP OF WHITE SNAKEROOT TO MILK SICKNESS OR "TREMBLES." *U. S. Dept. Agr., Bur. Plant Indus. Bul.* 121: 5-20, illus. 1908.

sults were obtained by others, among whom especial mention should be made of Wolf, Curtis, and Kaupp.⁶

Too much credit, however, for proving the connection of white snakeroot with trembles should not be given to the work of recent years, for John Rowe in 1839 not only poisoned cattle and poisoned a calf from the milk of an affected cow by feeding the plant, but also got affidavits from responsible people, who were acquainted with the symptoms of trembles, declaring that his experimental animals had the disease. W. J. Vermilya, in 1859, too, poisoned sheep and horses experimentally. These experiments by Rowe and Vermilya were just

as conclusive as anything done in this century, but did not receive the recognition which was their due.

At the present time it is known that the feeding of herbivorous animals on white snakeroot may produce poisoning with the typical symptoms which have been known since early in the nineteenth century. (Fig. 1.) Not only are animals poisoned by eating the plant, but it has been shown experimentally that milk from poisoned animals may produce the disease in their offspring (fig. 2) or

characteristic attitude,

FIGURE 1.—A sheep poisoned by white snakeroot. The indistinctness of the picture of the animal was caused by its violent trembling—one of the symptoms of the disease. Note the clearness of the wheel behind the sheep.

other animals. The cover illustration shows a due to weakness of the forelegs.

When white snakeroot is dried it gradually loses much of its power of producing the disease.

ANIMALS POISONED

It seems probable that none of our common domestic animals are immune from the effect of the plant. The following have been poisoned experimentally by the plant: Cattle, horses, sheep, mules, swine, guinea pigs, chickens, and rabbits.

TRANSMISSION OF THE DISEASE BY MILK

The disease has been transmitted to calves, lambs, and young rabbits by the mothers of these animals. Cats have been poisoned by

⁶ WOLF, F. A., CURTIS, R. S., and KAUPP, B. F. A MONOGRAPH ON TREMBLES OR MILK SICKNESS AND WHITE SNAKE ROOT. N. C. Agr. Expt. Sta. Tech. Bul. 15, 75 p., illus. 1918.

milk from affected cows, and there are many more or less well-authenticated reports of the poisoning of other animals in the same manner. It is commonly reported that lactating cows may not show symptoms, although their calves are affected. Some even say that cows do not show symptoms so long as there is free lactation; this has been proved not to be true in all cases, but without much doubt calves are sometimes sick when their mothers show no definite symptoms.

MEAT OF POISONED ANIMALS

In the literature of the subject there are many accounts of the poisoning of dogs, cats, wolves, and other animals by the meat of diseased animals, and there are some definite experiments that apparently prove this. The experiments in feeding meat by the United States Department of Agriculture and by Wolf, Curtis, and Kaupp, however, were without effect.

TREMBLES OR MILK SICKNESS IN MAN

It is currently believed that human cases have arisen from consuming the milk or butter of cows affected by trembles. While, of course, definite experiments to test this belief are out of the question, the experience of large numbers of people, including many physicians, is fairly conclusive evidence that the belief is correct.

DESCRIPTION OF WHITE SNAKEROOT

Eupatorium uticæfolium Reichard (fig. 3), quoted as *E. ageratoides* L. in the older botanies, is a slender, erect, perennial herb, belonging to the family Compositæ. Its leaves, which are 3 to 5 inches long, are opposite, broadly ovate, pointed, sharply toothed and thin, and have rather long petioles. The small white flowers are in compound corymbs of 8 to 10 flowers, appearing late in the summer and fall. The plants are from 1 to 4 feet in height.

It is found widely distributed in the eastern United States and as far west as Minnesota, Nebraska, Oklahoma, and Louisiana. Its favorite habitat is in rich soil of damp woods. It is abundant in the groves along the watercourses of the Middle States and grows with especial profusion in the so-called coves, or damp, shaded ravines, of the northern slopes of the southern Appalachians. It is by no means, however, confined to shaded situations, for it sometimes grows in masses on cleared hillsides in the open.



FIGURE 2.—This calf was poisoned by the milk of its mother; the cow was poisoned by white snakeroot

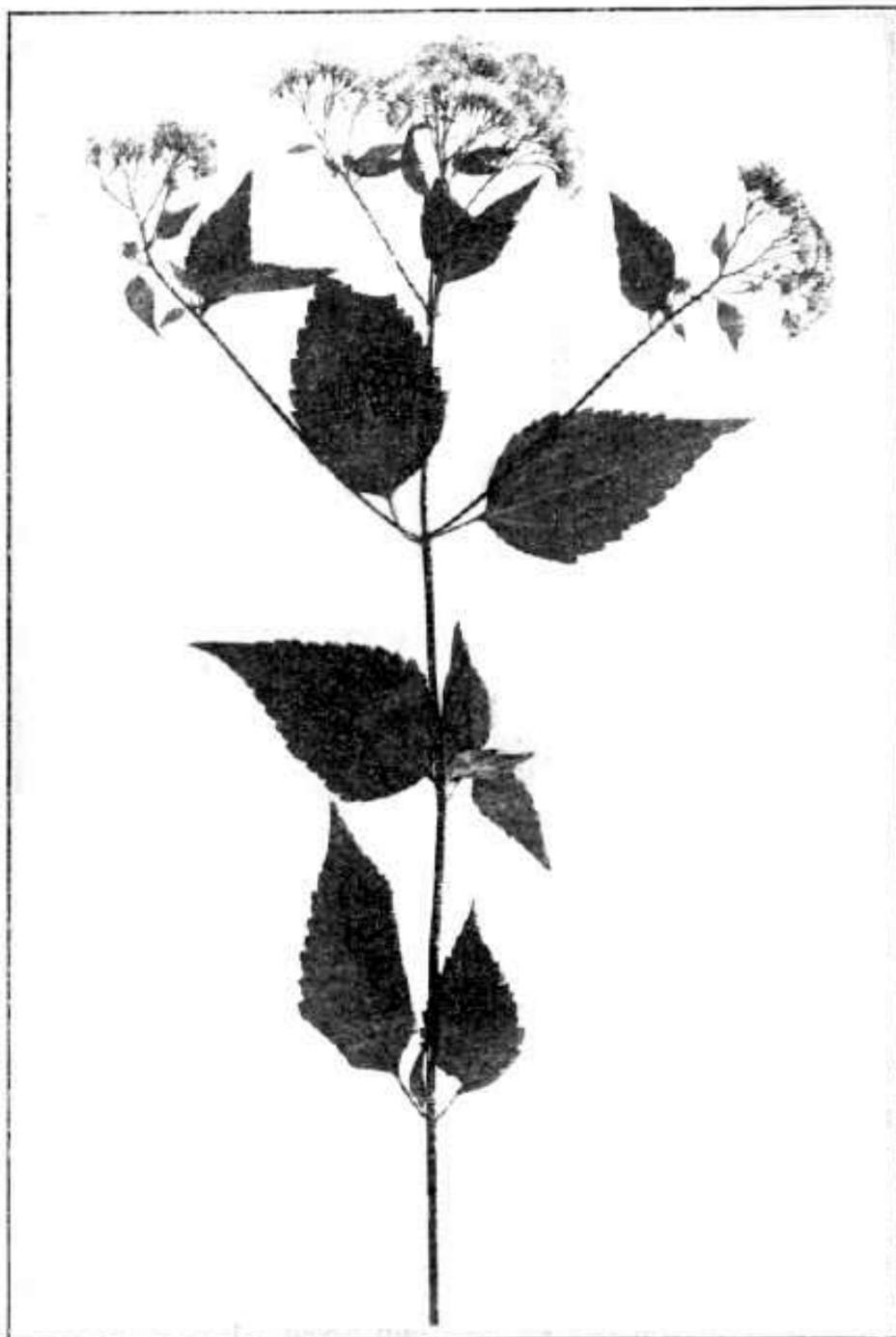


FIGURE 3.—White snakeroot (*Eupatorium urticaceum*)

It is most commonly known as white snakeroot. Other names which have been applied to it are white sanicle, Indian sanicle, deerwort, boneset, poolwort, poolroot, richweed, squawweed, whitetop, and steria.

The common thoroughwort, *Eupatorium perfoliatum* L., which grows in similar localities, but usually on soils with more moisture, is readily distinguished from *E. urticacefolium*, as it is a coarser plant and the leaves are long, narrow, rugose, and, as the name indicates, are without petioles and are united around the stem.

TREMBLES OR MILK SICKNESS FROM RAYLESS GOLDENROD

For many years there has been known in the Southwest, especially in the Pecos Valley, N. Mex., a disease, of man and domestic animals, commonly called "alkali disease" or "milk sickness." The latter term was applied because local physicians recognized a likeness in symptoms to the trembles or milk sickness of the East, and thought that the human cases were produced by the consumption of milk or butter from cows affected by the disease. Losses of animals, especially cattle, were reported and also many cases of sickness and death of people. The term "alkali disease" originated from the opinion held by many that alkali water was the cause. Jordan and Harris⁷ found in this region the same bacillus which they had discovered in the Central States. Here, however, as in the East, there was a persistent opinion held by many people that the cause was a plant, and that the suspected plant was the rayless goldenrod, or jimmy weed (*Aplopappus heterophyllus*).

The experimental proofs that white snakeroot is the real source of eastern trembles led the United States Department of Agriculture to make extended feeding tests with the rayless goldenrod. The results of these tests, showed conclusively the following facts:

The alkali disease or milk sickness of animals in the Pecos Valley is caused by feeding on the rayless goldenrod and affects cattle, horses, and sheep.

The disease is not of bacterial origin, because it is produced by sterilized plant.

The symptoms of the "alkali disease" can not be distinguished from those produced by white snakeroot. (Fig. 4.)



FIGURE 4.—This animal was in the last stages of the disease, which was caused by rayless goldenrod

⁷ JORDAN, E. O., and HARRIS, N. M. See p. 3.

The poison is conveyed by the milk of lactating animals (fig. 5) and reaches human beings through milk or butter.

DESCRIPTION OF RAYLESS GOLDENROD

Aplopappus heterophyllus (Gray) Blake, formerly known as *Iscocoma wrightii*, shown in Figure 6, belongs to the Composite family, in which the flowers are in compact heads, the heads being often mistaken for real flowers, as in the case of the sunflowers. It is commonly called rayless goldenrod, but in some localities the term "jimmy weed" is used.

The plant is a stout, erect, tufted perennial herb with shrubby or near-shrubby base, minutely hairy to nearly smooth, commonly from 1 to 2 feet in height, but sometimes under favorable circumstances

of growth, as on the banks of irrigating ditches, it may reach a height of 4 feet or even more.

The leaves are alternate, one-eighth to one-fourth inch wide, three-fourths to $2\frac{1}{2}$ inches long, usually with stout, stiff hairs on the margin, occasionally with short, sharp, scattered teeth, and acute or obtuse at the apex.

The heads are numerous, with or without



FIGURE 5.—A cow seriously affected by trembles, caused by rayless goldenrod; the calf in the foreground was made sick by the cow's milk.

out stems, in terminal flat-topped bunches; the bracts surrounding the flower heads are about one-eighth inch high, oblong, usually obtuse, with obscurely green tips. The heads have 7 to 15 tubular yellow flowers. The seeds are silky and small.

The plant is found from southern Colorado to the Texas Panhandle and south to Arizona, Sonora, and Chihuahua. It grows in great abundance in the irrigated portions of the Pecos Valley in New Mexico and Texas.

Recently it has been shown that another species of rayless goldenrod, *Aplopappus fruticosus* (Rose and Standley) Blake, growing in some abundance in Arizona, has poisonous properties identical with those of *A. heterophyllus*.

TOXIC PRINCIPLES PRODUCING TREMBLES

Especial interest attaches to the determination of the constituents in the plants which are the cause of the disease. Many investigators have experimented with extracts of white snakeroot, and some have attempted to show that certain definite substances were the poisonous principles. For several years chemical studies of both

white snakeroot and rayless goldenrod have been carried on by the United States Department of Agriculture, and recently,⁸ a substance has been separated which has been named tremetol. The disease has been produced in sheep by tremetol, developing an acidosis, and it is significant that tremetol gradually disappears as the plant is dried.

There have been no publications dealing with the chemical composition of the rayless goldenrod.

DANGER FROM USING MILK OR BUTTER FROM AFFECTED COWS

Milk or butter from cows affected with trembles may produce the disease in human beings. Such products should be avoided. It should be noted, however, that in a general milk supply or in creamy butter, the toxic substance is so largely diluted that it is hardly possible for it to be harmful. In the experimental work with the plants the disease appeared only after somewhat prolonged feedings. While there are statements that sickness has occurred in human beings after drinking comparatively small quantities of milk from diseased animals, it probably can be assumed that the disease results ordinarily from a continued use of milk or butter from animals affected by trembles. As a matter of fact, there is no recorded case of milk sickness in a city. All known cases have originated either on farms or from milk products supplied directly from farms.

REMEDIES

For human cases many forms of treatment have been recommended. Dr. W. E. Walsh, of Morris, Ill., who has had an exceptionally wide experience with the disease in his neighborhood and has diagnosed it as an acidosis, places great dependence on sodium bicarbonate, using with it milk of magnesia. He also gives enemas of sodium bicarbonate and glucose when the vomiting is incessant. These remedies he rightly considers logical.

For sick animals no effective remedial treatment is known. They may be benefited by laxatives or purgatives; for this Epsom salt or raw linseed oil may be used. The feed should be of a laxative character.

PREVENTION

In many places in the Eastern States trembles areas have been fenced off, with consequent prevention of losses. In some localities



FIGURE 6.—Rayless goldenrod

⁸ COUCH, J. F. THE TOXIC CONSTITUENT OF RICHWEED OR WHITE SNAKEROOT (EUPATORIUM URTICACEIFOLIUM). Jour. Agr. Research 35: 547-576, illus. 1927.

(fig. 7) where *Eupatorium urticæfolium* is particularly abundant this evidently is advisable. The clearing of land and seeding to corn, grain, or grasses will of course stop the trouble. It has long been known that trembles affects animals pastured on unbroken land and that the disease disappears after the land is cultivated.

So far as getting rid of the plant is concerned, however, one must remember that partial clearing is not sufficient. Although the plant favors damp and shaded places, it sometimes grows most luxuriantly on partially cleared land. It has been noticed in the mountains of North Carolina that the plant increases enormously in cleared land and disappears only after the land has been seeded down.

If an attempt is made to destroy white snakeroot in pastures, one should remember that it is a perennial and that consequently cutting down is not sufficient. It must be pulled up. Fortunately it does

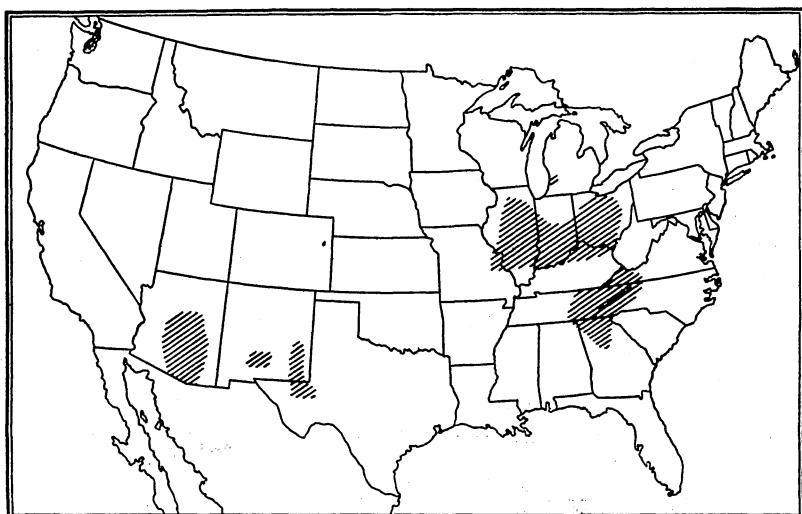


FIGURE 7.—Distribution of trembles in the United States. The cause in the eastern area is white snakeroot; in the western area it is rayless goldenrod.

not have an extensive root system, and it is possible to kill it out in this way.

Although the rayless goldenrod grows with great luxuriance in some places, it has been found entirely feasible to dig it out in pastures. When dug to a depth of 2 or 3 inches, the plant is killed, and a single thorough digging has been shown to be surprisingly effective.

As in the case of most stock-poisoning plants, neither white snakeroot nor rayless goldenrod is sought by animals. The plants are ordinarily eaten only when desirable forage is lacking. Cases of poisoning may occur when pastures are overgrazed or when animals are confined in places where the poisonous plants are especially abundant. It is evident that if the poisonous character of the plants is recognized, stock losses may be greatly reduced by so handling the animals that they do not graze largely in areas where these plants are especially abundant.